REMARKS

The Official Action of 24 February 2005 has been carefully considered and reconsideration of the application as amended is respectfully requested.

Claims 20, 22-30 and 36-45 stand rejected under 35 USC 112, first paragraph, for alleged failure to comply with the enablement requirement because the Examiner does not consider the evidence of record to show (a) the **prevention** of IDDM in the population as a whole or (b) the effectiveness of the recited vaccine in **high risk** individuals (as contrasted with the population as a whole). In response, Applicants have amended the claims from "a method of preventing. . . ." to "a method of reducing the risk of contracting" whereby to address the concern in (a). Support for this amendment appears in the specification as filed at, for example, pages 15 and 16, and the Examples beginning on page 16, and particularly page 24, first paragraph.

With respect to (b), Applicants respectfully note that the Examples in the specification beginning on page 16 provide evidence to show that OPV has a beneficial effect on immune protection against non-polio enterovirus infections and that this effect reduces the risk of complication of non-polio enterovirus infections like Type 1 diabetes. Accordingly, it is respectfully submitted that one of skill in the art would consider credible Applicants' presumptively accurate statements to this effect. Moreover, Applicants submit herewith the following test results which further support Applicants statements as to the utility of the claimed method for high risk individuals:

Summary of the OPV trial among children with increased genetic risk for type 1 diabetes

The protective effect of the proposed OPV vaccination regime was tested in children who were at increased genetic for type 1 diabetes. In this trial 64 children were immunized with OPV at early age according to the proposed immunization regime: Although 4 doses of OPV were given repeatedly to each child at the age of 2 months, 3 months, 6 months and 12 months. In addition, 700 control children were immunized with inactivated poliovirus vaccine (IPV) at an older age (at the age of 6 months, 12 months and 24 months). The OPV immunizations were carried out by using a commercially available OPV vaccine according to the standard per os protocol (one dose included two drops of vaccine given directly to the mouth). Each dose included a mixture of the three poliovirus Sabin strains (poliovirus 1, 2 and 3) in the following concentrations (TCID50): poliovirus 1: 10^6; poliovirus 2: 10^5; poliovirus 3: $10^{5.8}$. All immunized children carried HLA-genes, which increased their risk for type 1 diabetes, determined by the screening of the HLA-DQ alleles at birth. Recruited children carried the HLA-DQB1*302 risk allele but were negative for HLA-DQB1*0201, HLA-DQB1*0301 and HLA-DQB1*0602 alleles. All immunized children were followed from birth and serum samples were regularly taken at the age of 3 months, 6 months, 9 months, 12 months, 18 months, 24 months and then annually. The children were followed from birth for an average of 3.5 years in both groups.

The effect of OPV was analyzed by studying its effect on the appearance of beta-cell damaging autoimmune process. This process can be identified by the presence of autoantibodies in serum (islet-cell autoantibodies, insulin autoantibodies, GAD65-autoantibodies and IA-2 autoantibodies) and leads to clinical type 1 diabetes after a lab period ranging from some weeks/months to several years. These autoantibodies were measured from serum samples form all children in the OPV-immunized and in the control group. OPV-immunized children turned positive for these autoantibodies less frequently than control children. Altogether 4.5% of the OPV-immunized children turned positive for at least one of these autoantibodies during the observation compared to 10.0% of control children (p=0.05). The results show that the proposed OPV immunization can decrease the risk of autoimmune beta-cell damaging process in genetically susceptible individuals.

It is respectfully submitted that the evidence of record confirms the accuracy of Applicants' presumptively accurate disclosure, and that the specification as filed is enabling for the invention as now claimed. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 USC 112, first paragraph.

Claims 20, 22, 36-38, 40, 41, 43 and 44 stand rejected under 35 USC 102 (b), in the paragraph bridging pages 3 and 4 of the Official Action, based upon an alleged public use or sale of the invention in Finland. Applicants respectfully traverse this rejection and call the

Examiner's attention to the express provisions of 35 USC 102(b), which require that, to be a statutory bar under the provisions of the statute, the public use or sale must be **in the United States** (". . . .in public use or on sale in this country"). Accordingly, it is respectfully submitted that the rejection is inappropriate and should be withdrawn.

Claims 20, 22-24 and 36-45 stand rejected under 35 USC 102(b) as allegedly being anticipated by or, in the alternative, under 35 USC 103(a) as allegedly being obvious over the WHO Weekly Epidemiological Record. Applicants respectfully traverse these rejections.

All of the claims rejected in view of the WHO Weekly Epidemiological Record have now been amended to recite a selection step wherein the recited vaccine is administered only to selected high-risk groups (and not to the population as a whole). Support for this amendment appears in the specification as filed at, for example, page 14, lines 4-7. In contrast, the subject rejections are based on an inherency rationale: the Examiner considers that the population considered in the cited publication is so large as to guarantee that high-risk subpopulations are included. However, the Examiner has not alleged, and there is nothing in the cited reference that would suggest, the step of screening the population as a whole to select only those at high-risk for contracting Type I diabetes mellitus. In the absence of a motivation in the prior art to modify the cited reference to provide for a screening step, the cited art cannot set forth even a *prima facie* case of obviousness for the invention as now claimed (see MPEP Section 706.02(j)). Moreover, since the cited art does not show all of the claim limitations, it cannot be considered to anticipate the invention as now claimed (see MPEP Section 2112).

In view of the above, it is respectfully submitted that all rejections and objections of record have now been overcome and that the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

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